constituents, and resulting functional consequence (cell death) in the adjacent connected well.

Example 7—Hepatocyte—Cancer Cell Crosstalk

[0217] 20,000 primary human hepatocytes (Lonza) (Hepatocyte plating medium for 4 hours, followed by hepatocyte maintenance medium with 0.3% (v/v) matrigel GFR for 20 hours) or HepG2 cells (to be transfected with CYP2A6 cDNA (as per vendor's recommendation)) were plated in one well of the two connected wells in their respective cell culture medium (catalog number 3386 for Transwell® plate). Prior to plating the primary human hepatocytes from Lonza, the Transwell® plate was coated with 0.1 mg/ml collagen (50 μls) (C3867 Sigma—collagen I rat tail solution) (solubilized in 0.1% acetic acid in 1×PBS (v/v)) for 1 hour at 37° C. (cell culture incubator) and washed with 1×PBS. The primary human hepatocytes were sandwiched in the human hepatocyte maintenance medium with 0.3% matrigel GFR (v/v) for the next 20 hours.

[0218] In the other connected well of each test unit, 20,000 HCT116 cells were plated directly on the Transwell® membrane in McCoy's 5A media. For HepG2 cells, the cells were transfected with CYP2A6 cDNA for 48 hours prior to any drug addition. On the day of drug addition, the HCT116 colorectal cancer cells were moved into hepatocyte media in order to prevent mixing of different mediums.

[0219] The high-throughput microfluidic device illustrated in FIG. **5**B was cleaned, assembled and sterilized via autoclaving for 60 minutes. The wells of the autoclave-sterilized high-throughput microfluidic device (with two wells connected for each test unit) were filled with 300 μLs of media and centrifuged at 40 r.c.f for 4 minutes to fill all the flow channels. Transwell® plates with the cells adhered on the upper side of the membrane (inside the well) were carefully lowered into the channels and pressed in to make seamless contact with the microfluidic channel. FIG. **12**A depicts how the wells are filled, and FIG. **12**B illustrates a test unit of the system.

[0220] Next, different concentrations of prodrug Tegafur, a prodrug of 5FU (5-Fluorouracil), were added to the hepatocyte chamber, and fluidic flow was triggered for 72 hours. The device was placed on compressed air system and the fluid was pumped via membrane flexion under a compressed air of 1.5 psi (amplitude), sinusoidal wave pattern with a frequency of 0.2. Media was refreshed every 24 hours via the vertical channel with flared opening. The flared opening allowed easy physical and visual access into the constituents of the microfluidic channel in order to ensure proper filling. The cells were imaged with live/dead staining after 72 hours to understand the prodrug metabolism and resulting cell death in the HCT116 cells.

[0221] As seen in FIG. **12**C, the first panel shows high viability of Hepatocytes was retained after drug treatment, with a slight dose dependent increase in the propidium iodide stain in the hepatocytes. However, the HCT116 eGFP cells in the connected wells showed significant dose dependent toxicity with increasing concentrations of Tegafur (second panel of FIG. **12**C).

[0222] These results demonstrate the usability of the high-throughput multi-organ microfluidic device for complex biological experiments such as prodrug metabolization in one simulated organ (a first well) accompanied by cell death in a susceptible cell population in a second simulated organ (second well), where the drug liberated by cells in the first well resulted in death of cells in the second well.

Example 8—Proximal Tubule Cell Culture on the Underside of the Transwell® Membrane Under Static Conditions and Shear Conditions

[0223] Human proximal tubule epithelial cells (PTECs) are grown to confluence in a collagen I coated T75 flask in ATCC media before the experiment. ATCC media—Renal Epithelial Cell Basal Medium (ATCC® PCS-400-030™) is mixed with Renal Epithelial Cell Growth Kit (ATCC® PCS-400-040™) containing—Triiodothyronine: 10 nM, rh EGF: 10 ng/mL, Hydrocortisone Hemisuccinate: 100 ng/mL, rh Insulin: 5 μg/mL, Epinephrine: 1 μM, L-Alanyl-L-Glutamine: 2.4 mM, Transferrin: 5 μg/ml Fetal bovine serum (FBS): 0.5% as per vendor's recommendations.

[0224] Transwell® insert membrane of 96 w corning plates were coated with 0.01% rat tail collagen (Sigma: C3867) (diluted in sterile cell culture grade water) by incubating the wells on a rocker for 6 hours at room temperature followed by their incubation overnight at 4° C. After rinsing the membranes with 1×PBS, 200,000 human PTECs/cm^2 (Primary Renal Proximal Tubule Epithelial Cells; Normal, Human (RPTEC) (ATCC® PCS-400-010™)) were added to the Transwell® membrane in 10 μL media and allowed to adhere to the membrane for 4 hours. The cells were then incubated with 200 μLs of media for 48 hours before the static culture.

[0225] For the fluidic shear experiments, the human PTECs were grown on the underside of the membrane for 6 days before transferring to the high throughput microfluidic device. A shear of 0.1-0.2 dynes/cm^2 was provided for a time period of 12 hours via rhythmic flexion of the flexible membrane of the device, followed by testing the PTEC cells for their viability.

[0226] Prior to the static or fluidic experiments, the high-throughput microfluidic device was cleaned, assembled and sterilized via autoclaving for 60 minutes. The wells of the autoclave sterilized high-throughput microfluidic device (two-well connects) were filled with 300 μLs of media and centrifuged at 40 r.c.f for 4 minutes to fill all the channels. Transwell® plates with the cells adhered to the underside of the membrane were carefully lowered into the channels and pressed in to make seamless contact with the microfluidic channel for 48 hours (static conditions) or 12 hours (fluidic shear conditions) followed by staining with calcein AM to qualitatively estimate the viability. Cells grown on the underside of a similarly prepared Transwell® membrane that wasn't inserted into the high throughput microfluidic device were used as a control for the experiment.

[0227] Cells cultured on the underside of the Transwell® membrane and transferred into the high throughput microfluidic device showed similar viability as compared to the control well that was not transferred (FIG. **13**A). Cells exposed to fluid shear for 12 hours also showed similar viability to cells on the control membrane (FIG. **13**B). This demonstrates that the microfluidic device can be used to expose healthy, live cells to shear flow conditions for testing as described herein.

What is claimed is:

1. A fluidic device comprising:

a manifold body comprising a substantially flat horizontal top surface, two or more separated flow channels, each of said flow channels having a horizontal section with